Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptansc1625

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

| | | |
|---|---|---|
| NEWS 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS 2 | JUL 02 | LMEDLINE coverage updated |
| NEWS 3 | JUL 02 | SCISEARCH enhanced with complete author names |
| NEWS 4 | JUL 02 | CHEMCATS accession numbers revised |
| NEWS 5 | JUL 02 | CA/CAplus enhanced with utility model patents from China |
| NEWS 6 | JUL 16 | CAplus enhanced with French and German abstracts |
| NEWS 7 | JUL 18 | CA/CAplus patent coverage enhanced |
| NEWS 8 | JUL 26 | USPATFULL/USPAT2 enhanced with IPC reclassification |
| NEWS 9 | JUL 30 | USGENE now available on STN |
| NEWS 10 | AUG 06 | CAS REGISTRY enhanced with new experimental property tags |
| NEWS 11 | AUG 06 | BEILSTEIN updated with new compounds |
| NEWS 12 | AUG 06 | FSTA enhanced with new thesaurus edition |
| NEWS 13 | AUG 13 | CA/CAplus enhanced with additional kind codes for granted patents |
| NEWS 14 | AUG 20 | CA/CAplus enhanced with CAS indexing in pre-1907 records |
| NEWS 15 | AUG 27 | Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB |
| NEWS 16 | AUG 27 | USPATOLD now available on STN |
| NEWS 17 | AUG 28 | CAS REGISTRY enhanced with additional experimental spectral property data |
| NEWS 18 | SEP 07 | STN AnaVist, Version 2.0, now available with Derwent World Patents Index |
| NEWS 19 | SEP 13 | FORIS renamed to SOFIS |
| NEWS 20 | SEP 13 | INPADOCDB enhanced with monthly SDI frequency |
| NEWS 21 | SEP 17 | CA/CAplus enhanced with printed CA page images from 1967-1998 |
| NEWS 22 | SEP 17 | CAplus coverage extended to include traditional medicine patents |
| NEWS 23 | SEP 24 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

| | |
|---|---|
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |

Enter NEWS followed by the item number or name to see news on that specific topic.

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research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:36:31 ON 28 SEP 2007

=> fil casreact

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'CASREACT' ENTERED AT 18:36:44 ON 28 SEP 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT


FILE CONTENT:1840 - 22 Sep 2007 VOL 147 ISS 14

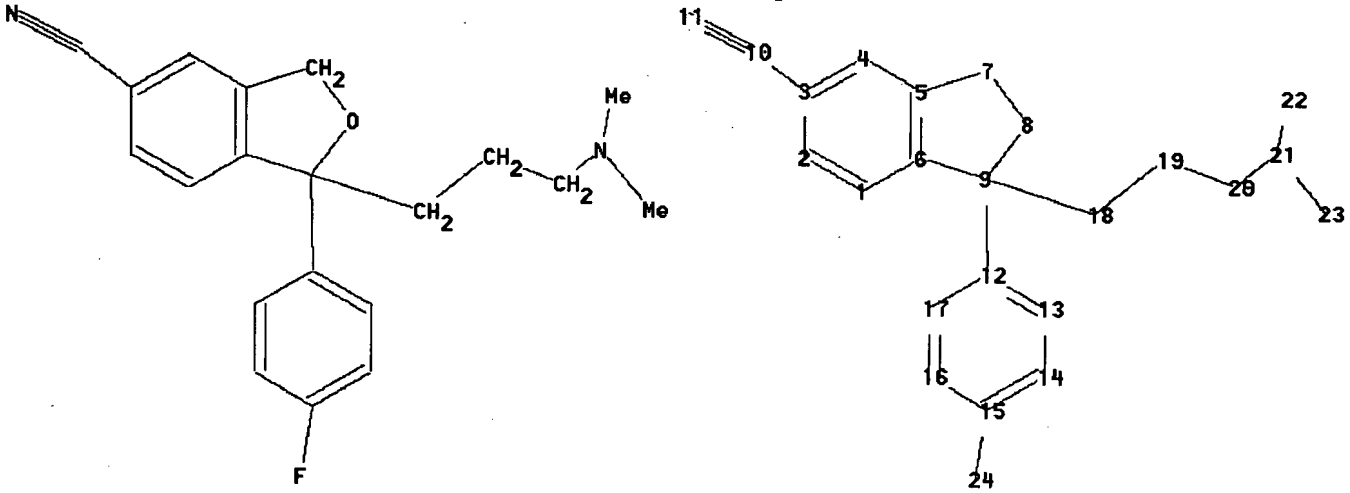
New CAS Information Use Policies, enter HELP USAGETERMS for details.

**********
*
*  CASREACT now has more than 12 million reactions
*
**********

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
Uploading C:\Program Files\Stnexp\Queries\citalopramA.str



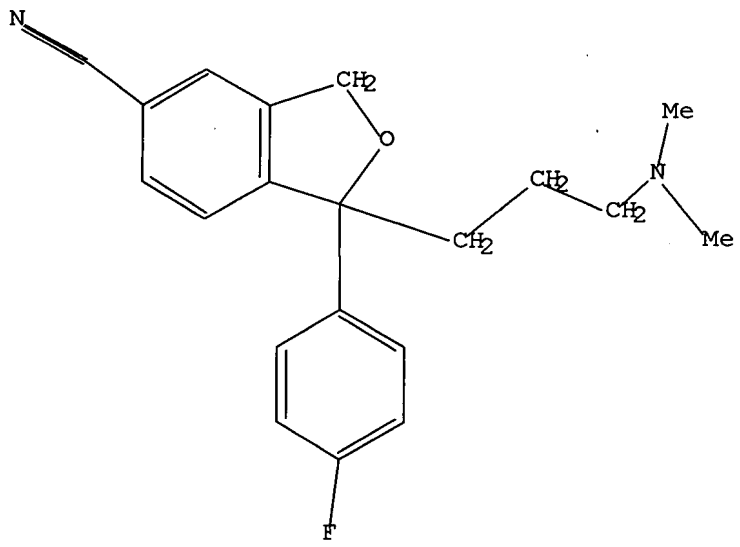

chain nodes :
10 11 18 19 20 21 22 23 24

ring nodes :
1 2 3 4 5 6 7 8 9 12 13 14 15 16 17
chain bonds :
3-10 9-12 9-18 10-11 15-24 18-19 19-20 20-21 21-22 21-23
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 12-13 12-17 13-14 14-15 15-16
16-17
exact/norm bonds :
5-7 6-9 7-8 8-9 10-11
exact bonds :
3-10 9-12 9-18 15-24 18-19 19-20 20-21 21-22 21-23
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS
fragments assigned product role:
containing 1

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR




Structure attributes must be viewed using STN Express query preparation.

=> s sss sam l1
SAMPLE SEARCH INITIATED 18:37:54 FILE 'CASREACT'
SCREENING COMPLETE - 28 REACTIONS TO VERIFY FROM 5 DOCUMENTS

100.0% DONE 28 VERIFIED 28 HIT RXNS 5 DOCS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 243 TO 877
PROJECTED ANSWERS: 5 TO 234

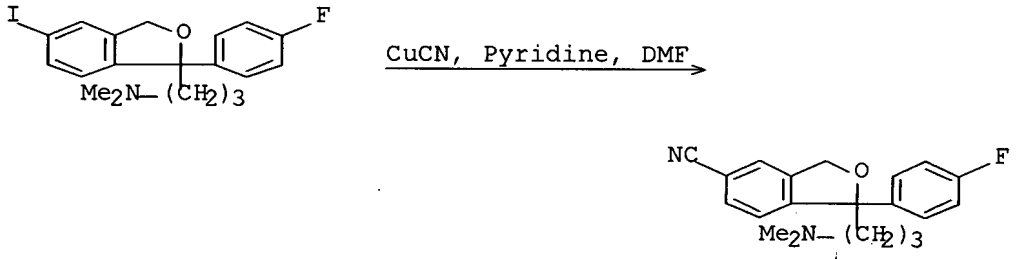
L2 5 SEA SSS SAM L1 ( 28 REACTIONS)

=> d scan

L2 5 ANSWERS CASREACT COPYRIGHT 2007 ACS on STN

TI Processes for the preparation of citalopram and its intermediate from 5-aminophthalide

RX(4) OF 15




ALL ANSWERS HAVE BEEN SCANNED

=> fil stng
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 1.35 | 1.56 |

FILE 'STNGUIDE' ENTERED AT 18:38:21 ON 28 SEP 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 24, 2007 (20070924/UP).

=> s sss l1 full
SUBSTANCE QUERIES NOT VALID IN THIS FILE
The logic expression entered contains L#s or saved query names which correspond to structures built by the STRUCTURE command or to screen sets. These must be searched in a substance file such as the REGISTRY file. In some files you may use a Registry Number answer set from a structure search as a search term or profile in some bibliographic file containing Registry Numbers, e.g. the CA file. For an explanation, enter "HELP CROSSOVER" at an arrow prompt (=>).

=> fil casreact
COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.90 | 2.46 |

FILE 'CASREACT' ENTERED AT 18:47:09 ON 28 SEP 2007

FILE CONTENT:1840 - 22 Sep 2007 VOL 147 ISS 14

New CAS Information Use Policies, enter HELP USAGETERMS for details.

**********
*
*  CASREACT now has more than 12 million reactions
*
**********

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

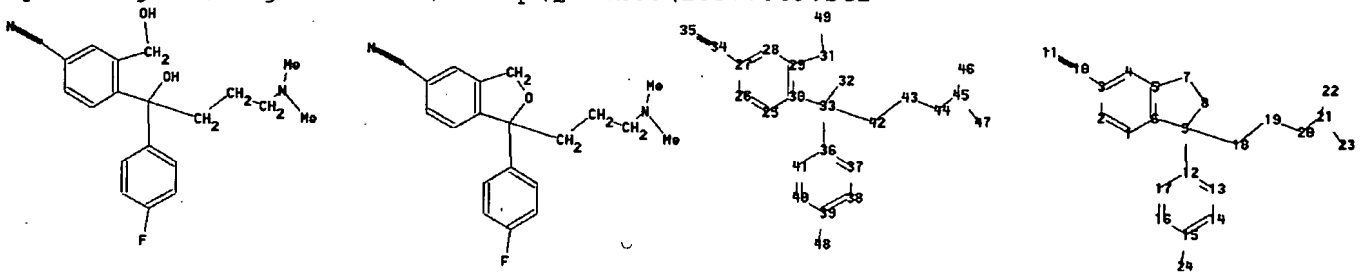
=> s sss l1 full
FULL SEARCH INITIATED 18:47:24 FILE 'CASREACT'
SCREENING COMPLETE - 323 REACTIONS TO VERIFY FROM 76 DOCUMENTS

100.0% DONE 323 VERIFIED 271 HIT RXNS 72 DOCS
SEARCH TIME: 00.00.01

L3 72 SEA SSS FUL L1 ( 271 REACTIONS)

=> save l3 citalopram07/A
ANSWER SET L3 HAS BEEN SAVED AS 'CITALOPRAM07/A'

=>
Uploading C:\Program Files\Stnexp\Queries\10577869.str



chain nodes :
10 11 18 19 20 21 22 23 24 31 32 33 34 35 42 43 44 45 46 47 48 49
ring nodes :
1 2 3 4 5 6 7 8 9 12 13 14 15 16 17 25 26 27 28 29 30 36 37 38 39 40 41
chain bonds :
3-10 9-12 9-18 10-11 15-24 18-19 19-20 20-21 21-22 21-23 27-34 29-31 30-33 31-49 32-33 33-36 33-42 34-35 39-48 42-43 43-44 44-45 45-46 45-47
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 12-13 12-17 13-14 14-15 15-16

16-17 25-26 25-30 26-27 27-28 28-29 29-30 36-37 36-41 37-38 38-39 39-40
40-41
exact/norm bonds :
5-7 6-9 7-8 8-9 10-11 32-33 34-35
exact bonds :
3-10 9-12 9-18 15-24 18-19 19-20 20-21 21-22 21-23 27-34 29-31 30-33
31-49 33-36 33-42 39-48 42-43 43-44 44-45 45-46 45-47
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17 25-26 25-
30 26-27 27-28 28-29 29-30 36-37 36-41 37-38 38-39 39-40 40-41

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:CLASS 35:CLASS 36:Atom
37:Atom 38:Atom 39:Atom 40:Atom 41:Atom 42:CLASS 43:CLASS 44:CLASS 45:CLASS
46:CLASS 47:CLASS 48:CLASS 49:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 25

L4 STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS
L4 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l4 sss subset=l3 sam
SAMPLE SUBSET SEARCH INITIATED 18:49:07 FILE 'CASREACT'
SCREENING COMPLETE - 0 REACTIONS TO VERIFY FROM 0 DOCUMENTS

100.0% DONE 0 VERIFIED 0 HIT RXNS 0 DOCS
SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET): ONLINE **COMPLETE**
PROJECTED VERIFICATIONS (WITHIN SPECIFIED SUBSET): 0 TO 0
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET): 0 TO 0

L5 0 SEA SUB=L3 SSS SAM L4 ( 0 REACTIONS)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d his

(FILE 'HOME' ENTERED AT 18:36:31 ON 28 SEP 2007)

FILE 'CASREACT' ENTERED AT 18:36:44 ON 28 SEP 2007

```
L1              STRUCTURE UPLOADED
L2            5 S SSS SAM L1

     FILE 'STNGUIDE' ENTERED AT 18:38:21 ON 28 SEP 2007

     FILE 'CASREACT' ENTERED AT 18:47:09 ON 28 SEP 2007
L3           72 S SSS L1 FULL
                SAVE L3 CITALOPRAM07/A
L4              STRUCTURE UPLOADED
L5            0 S L4 SSS SAM SUB=L3

=> s l4 subset=l3 sam
SAMPLE SUBSET SEARCH INITIATED 18:50:44 FILE 'CASREACT'
SCREENING COMPLETE -        0 REACTIONS TO VERIFY FROM        0 DOCUMENTS

100.0% DONE       0 VERIFIED       0 HIT RXNS                       0 DOCS
SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET):           ONLINE  **COMPLETE**
PROJECTED VERIFICATIONS (WITHIN SPECIFIED SUBSET):       0 TO        0
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET):             0 TO        0

L6            0 SEA SUB=L3 SSS SAM L4 (     0 REACTIONS)

=> s l4 subset=l3 full
FULL SUBSET SEARCH INITIATED 18:51:16 FILE 'CASREACT'
SCREENING COMPLETE -       44 REACTIONS TO VERIFY FROM       17 DOCUMENTS

100.0% DONE      44 VERIFIED      27 HIT RXNS                      14 DOCS
SEARCH TIME: 00.00.01

L7           14 SEA SUB=L3 SSS FUL L4 (    27 REACTIONS)

=> d ibib abs hit 1-14


L7   ANSWER 1 OF 14  CASREACT  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         147:211613  CASREACT  Full-text
TITLE:                    Process for asymmetric alkylation of carbonyl
                          compounds
INVENTOR(S):              Albert, Martin; Sturm, Hubert; Berger, Andreas;
                          Kremminger, Peter
PATENT ASSIGNEE(S):       Sandoz A.-G., Switz.
SOURCE:                   PCT Int. Appl., 36pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ----------------  ----  --------       ---------------  --------
     WO 2007082771      A1   20070726       WO 2007-EP516    20070122
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
             KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
```

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

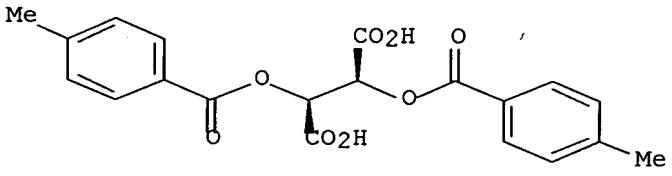
PRIORITY APPLN. INFO.: GB 2006-1286 20060123

OTHER SOURCE(S): MARPAT 147:211613

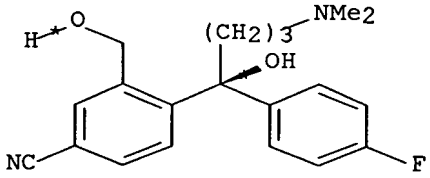
AB This invention relates to a process for stereoselective alkylation of carbonyl groups comprising reaction of a carbonyl compound (containing an anchor group capable of reacting with a boric or boronic acid derivs.) with an organometallic compound in the presence of a chiral alc. and a boron compound For example, 4-(4-fluorobenzoyl)-3-(hydroxymethyl)benzonitrile was reacted with (1S,2S)-N-methylpseudoephedrine and diisopropoxymethylborane, followed by the addition of dimethylaminopropyl magnesium chloride to give (S)-4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxymethyl)benzonitrile with 90.0% enantiomeric excess. The chiral tertiary alc. obtained in the previous step is an useful intermediate for synthesizing antidepressant drug Escitalopram.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

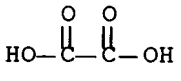
RX(8) OF 24 ...D + Y ===> Z



D: CM 1

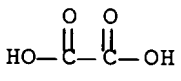


D: CM 2

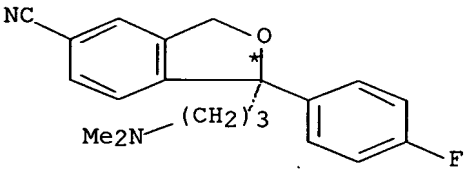


Y

(8)



Z: CM 1



Z: CM 2

RX(8) RCT D 128173-53-5

STAGE(1)
RGT AA 7664-41-7 NH3
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
CON room temperature, pH 9

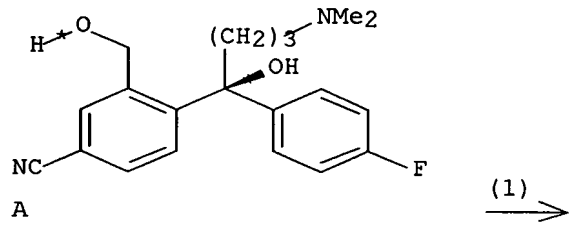
STAGE(2)
RGT AB 121-44-8 Et3N, AC 104-15-4 TsOH
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 1 hour, <5 deg C

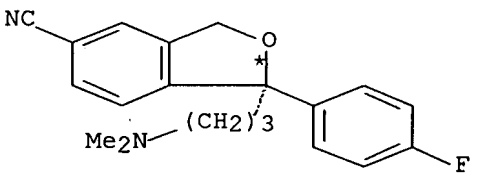
STAGE(3)
RCT Y 144-62-7

PRO Z 219861-08-2
NTE stereoselective

L7 ANSWER 2 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:500809 CASREACT Full-text
TITLE: An improved resolution process for the preparation of antidepressant drug: escitalopram
AUTHOR(S): Mital, Alka; Kumar, Rakesh; Ramachandran, Uma
CORPORATE SOURCE: Department of Pharmaceutical Technology, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, 160062, India
SOURCE: Organic Preparations and Procedures International (2006), 38(4), 423-426
CODEN: OPPIAK; ISSN: 0030-4948
PUBLISHER: Organic Preparations and Procedures, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Efficient resolution process for the intermediate racemic diol 4-(4-dimethylamino)-1-(4'-fluorophenyl)-1-(hydroxybutyl)-3-(hydroxymethyl)benzonitrile, wherein the S-diol is obtained in pure form, which is basified and then cyclized to give S-citalopram of >99 % enantiomeric purity. The method provides an easy way to improve the enantiomeric purity of S-citalopram that is obtained by diastereomeric salt crystallization method as compared to the other processes. The novelty of this process is that the enriched diastereomeric salt is crystallized twice using a medium polar solvent, before it is released as a free base. This avoids the cumbersome two stage purification process of the other reported processes.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 10 ...A ===> B

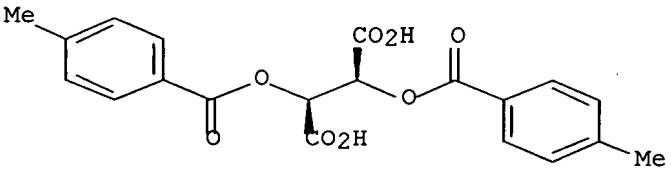




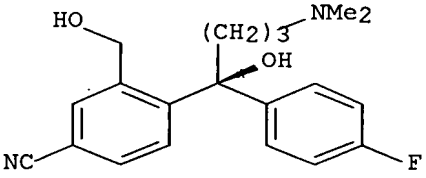
B
YIELD 70%

RX(1) RCT A 488787-59-3
RGT C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
PRO B 128196-01-0
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 10 minutes, 0 deg C
SUBSTAGE(2) 3 hours, 0 deg C

RX(7) OF 10 COMPOSED OF RX(4), RX(1)
RX(7) K ===> B

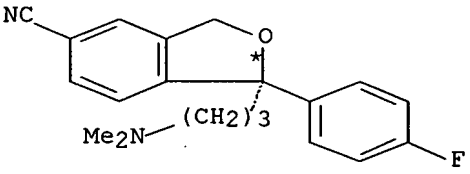


K: CM 1



K: CM 2

2
STEPS

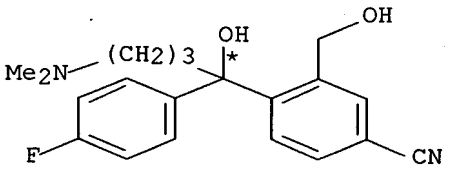


B
YIELD 70%

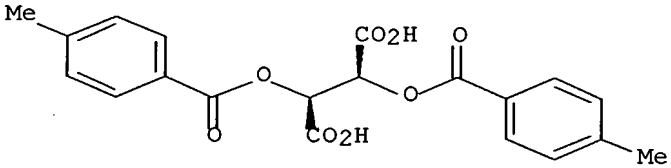
RX(4)  RCT  K 128173-53-5
       RGT  M 144-55-8 NaHCO3
       PRO  A 488787-59-3
       SOL  7732-18-5 Water
       CON  room temperature

RX(1)  RCT  A 488787-59-3
       RGT  C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
       PRO  B 128196-01-0
       SOL  108-88-3 PhMe
       CON  SUBSTAGE(1) 10 minutes, 0 deg C
            SUBSTAGE(2) 3 hours, 0 deg C

RX(9) OF 10 COMPOSED OF RX(3), RX(4), RX(1)
RX(9)  G + J ===> B

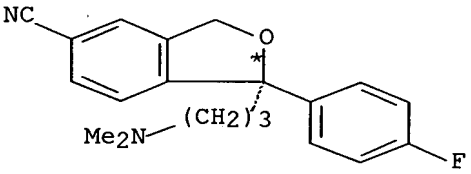



G




J

3
STEPS



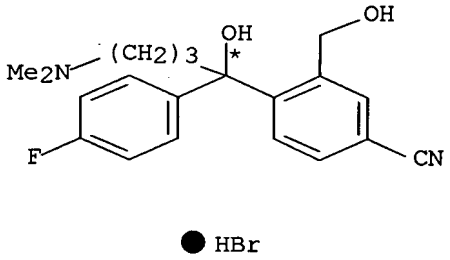

B
YIELD 70%

RX(3)  RCT  G 103146-25-4, J 32634-68-7
       PRO  K 128173-53-5
       SOL  67-63-0 Me2CHOH
       CON  5 hours, 40 deg C

RX(4)  RCT  K 128173-53-5
       RGT  M 144-55-8 NaHCO3
       PRO  A 488787-59-3
       SOL  7732-18-5 Water
       CON  room temperature

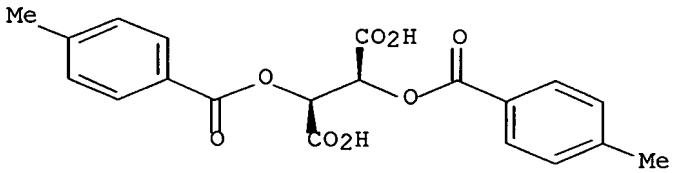
RX(1)  RCT  A 488787-59-3
       RGT  C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
       PRO  B 128196-01-0
       SOL  108-88-3 PhMe
       CON  SUBSTAGE(1) 10 minutes, 0 deg C
            SUBSTAGE(2) 3 hours, 0 deg C

RX(10) OF 10 COMPOSED OF RX(2), RX(3), RX(4), RX(1)
RX(10)  F + J ===> B



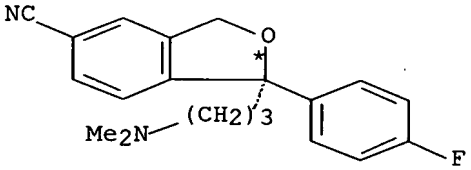

● HBr

F




J

4
STEPS
⟶




B
YIELD 70%

RX(2)  RCT  F 103146-26-5

RGT H 1310-73-2 NaOH
PRO G 103146-25-4
SOL 7732-18-5 Water, 108-88-3 PhMe
CON 15 minutes, 0 deg C

RX(3) RCT G 103146-25-4, J 32634-68-7
PRO K 128173-53-5
SOL 67-63-0 Me2CHOH
CON 5 hours, 40 deg C

RX(4) RCT K 128173-53-5
RGT M 144-55-8 NaHCO3
PRO A 488787-59-3
SOL 7732-18-5 Water
CON room temperature

RX(1) RCT A 488787-59-3
RGT C 121-44-8 Et3N, D 124-63-0 MeSO2Cl
PRO B 128196-01-0
SOL 108-88-3 PhMe
CON SUBSTAGE(1) 10 minutes, 0 deg C
SUBSTAGE(2) 3 hours, 0 deg C

L7 ANSWER 3 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:206191 CASREACT Full-text
TITLE: An improved process for preparation of escitalopram
INVENTOR(S): Kaushik, Vipin Kumar; Khan, Mohammed Umar; Meenakshisunderam, Sivakumaran
PATENT ASSIGNEE(S): Aurobindo Pharma Limited, India
SOURCE: PCT Int. Appl., 18pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

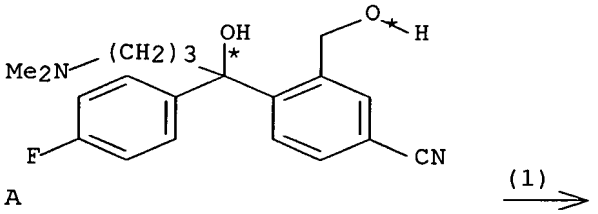
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007012954 | A1 | 20070201 | WO 2006-IB2050 | 20060720 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| IN 2005CH01014 | A | 20070720 | IN 2005-CH1014 | 20050727 |

PRIORITY APPLN. INFO.: IN 2005-CH1014 20050727

AB The present invention relates to an improved process for the preparation of escitalopram, which comprises purification and optical resolution of 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile to obtain the S-enantiomer, followed by cyclization to give escitalopram with 99.12% purity. The process has the advantages of high yield and high purity.

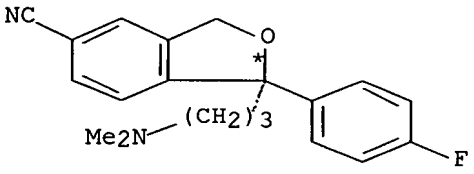
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 A ===> B




A

(1)




B

RX(1) RCT A 103146-25-4

STAGE(1)
RGT C 144-62-7 (CO2H)2
SOL 64-17-5 EtOH
CON SUBSTAGE(1) room temperature -> 55 deg C
SUBSTAGE(3) 15 - 20 deg C
SUBSTAGE(4) 4 hours

STAGE(2)
RGT D 7664-41-7 NH3
SOL 108-88-3 PhMe, 7732-18-5 Water
CON 30 - 35 deg C, pH 9.8

STAGE(3)
RGT E 32634-68-7 Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 50 - 55 deg C
SUBSTAGE(3) 25 - 30 deg C
SUBSTAGE(4) 10 hours

STAGE(4)
RGT F 124-63-0 MeSO2Cl, G 121-44-8 Et3N
CON SUBSTAGE(2) 3 hours, -10 - -5 deg C

PRO B 128196-01-0

L7 ANSWER 4 OF 14 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 146:80528 CASREACT Full-text
TITLE: Chemoenzymatic process for the synthesis of escitalopram
INVENTOR(S): Cotticelli, Giovanni; Salvetti, Raul; Bertoni, Chiara
PATENT ASSIGNEE(S): Adorkem Technology SpA, Italy
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006136521 | A1 | 20061228 | WO 2006-EP63193 | 20060614 |
| WO 2006136521 | A8 | 20070308 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | | |
|---|---|---|---|---|
| EP 1736550 | A1 | 20061227 | EP 2005-425452 | 20050622 |

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU

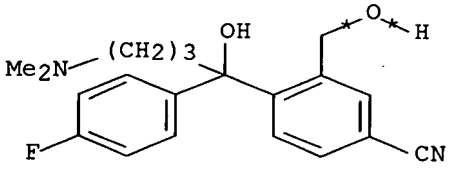
PRIORITY APPLN. INFO.: EP 2005-425452 20050622
US 2005-697398P 20050706

OTHER SOURCE(S): MARPAT 146:80528

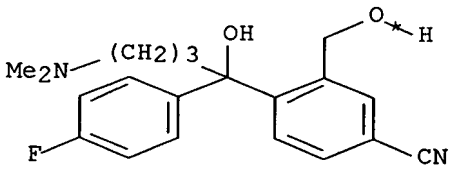
AB A process is described for the preparation of escitalopram and the pharmaceutically acceptable salts thereof starting from 5-cyanophthalide by a process which provides an enantioselective enzymic deacylation reaction of a complex of the formula (IV) where R represents a C1-C4 alkyl residue or an aryl residue under the action of an esterase from Aspergillus niger.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

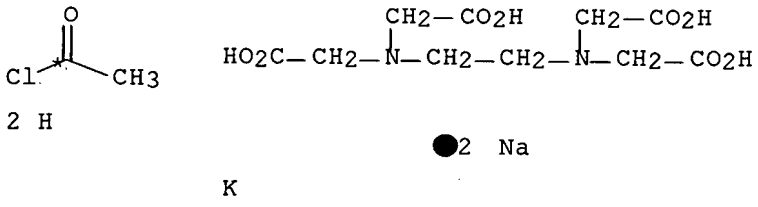
RX(26) OF 27 COMPOSED OF RX(2), RX(3), RX(4), RX(6), RX(7)
RX(26) 2 D + 2 H + K ===> U

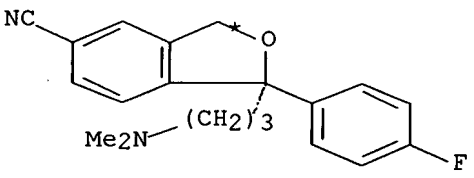



D




D




U

RX(2) RCT D 103146-25-4, H 75-36-5
PRO I 917476-35-8
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 35 - 40 deg C
SUBSTAGE(2) 35 - 40 deg C
NTE hundred gram scale, regioselective

RX(3) RCT I 917476-35-8

STAGE(1)
SOL 64-17-5 EtOH
CON room temperature

STAGE(2)
RCT K 139-33-3
SOL 7732-18-5 Water
CON room temperature

PRO L 917476-34-7
NTE hundred gram scale

RX(4) RCT L 917476-34-7

STAGE(1)
RGT P 7647-01-0 HCl
SOL 64-17-5 EtOH, 7732-18-5 Water
CON room temperature, pH 6

STAGE(2)
CAT 9001-62-1 Lipase
CON room temperature, pH 6

PRO N 917479-14-2, O 674806-13-4
NTE biotransformation, enzymic(lipase from Aspergillus niger immobilized on epoxy resin used), buffered solution(monobasic sodium phosphate), hundred gram scale, stereoselective

RX(6) RCT N 917479-14-2
RGT S 7664-41-7 NH3
PRO R 674806-14-5
SOL 7732-18-5 Water, 67-56-1 MeOH
CON 3 hours, room temperature
NTE gram scale

RX(7) RCT R 674806-14-5

STAGE(1)
RGT V 124-63-0 MeSO2Cl
SOL 108-88-3 PhMe
CON 10 minutes, 0 deg C

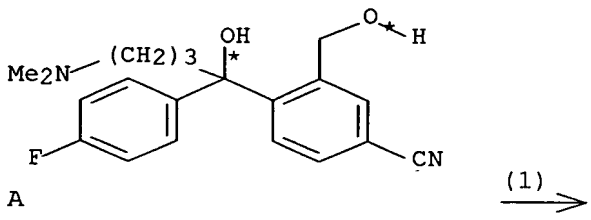
STAGE(2)
RGT W 121-44-8 Et3N
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 2 hours, 0 deg C

PRO U 128196-01-0
NTE alternative preparation shown, gram scale

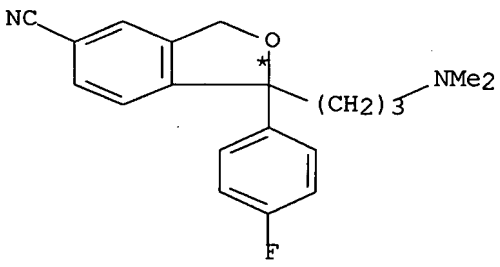
L7 ANSWER 5 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:335870 CASREACT Full-text
TITLE: Synthesis of citalopram hydrobromide
AUTHOR(S): Wu, Qiuye; Liao, Hongli; Zhao, Huiqing; Ye, Guangming; Jin, Yongsheng
CORPORATE SOURCE: School of Pharmacy, Second Military Medical University, Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2005), 36(1), 6-8
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Citalopram hydrobromide [i.e., 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile monohydrobromide] was synthesized from terephthalic acid and paraformaldehyde by condensation to give 5-carboxyphthalanone, which subjected to condensation, amidation and dehydration to afford 5-cyanophthalanone followed by twice Grignard reaction, cyclization and then salification with an overall yield of 31%.

RX(1) OF 10 ...A ===> B




A




● HBr

B
YIELD 78%

RX(1) RCT A 103146-25-4

STAGE(1)
RGT C 7664-93-9 H2SO4
SOL 7732-18-5 Water, 108-88-3 PhMe
CON SUBSTAGE(1) heated
SUBSTAGE(2) 3 hours, 80 deg C

STAGE(2)
RGT D 1336-21-6 NH4OH
SOL 7732-18-5 Water
CON room temperature, pH 10

STAGE(3)
RGT E 10035-10-6 HBr
CON cooled, pH 6 - 7

PRO B 59729-32-7
NTE HBr gas used in stage 3, overall yield 31%

L7 ANSWER 6 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:103520 CASREACT Full-text
TITLE: Preparation and purification of Citalopram salts
INVENTOR(S): Liu, Zhiping; Huang, Weipeng; Yuan, Aiguo; Xiao, Keqiang; Li, Youcheng; Zhuang, Jingfa
PATENT ASSIGNEE(S): Guangdong Xilong Chemical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

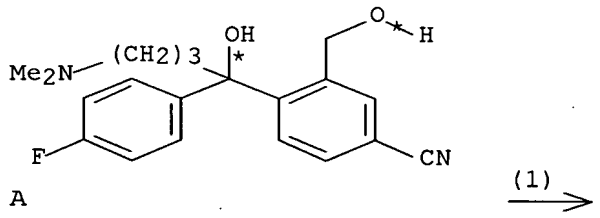
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| CN 1740167 | A | 20060301 | CN 2005-10035699 | 20050712 |

PRIORITY APPLN. INFO.: CN 2005-10035699 20050712

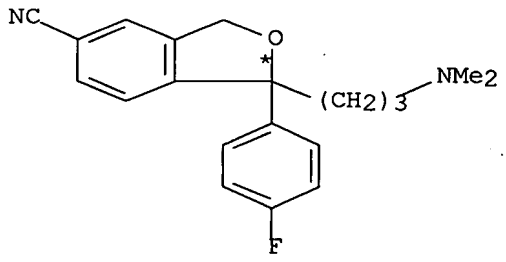
AB The invention provides a method for the preparation and purification of Citalopram salts, which comprises mixing an acid and Citalopram diol compound

at molar ratio of (1-10):1 in toluene at 50-100° under stirring, and recrystg. in water and the diluted acid to obtain corresponding Citalopram salts with a purity above 99.5%; wherein the acid can be hydrobromic acid, hydrochloric acid, hydroiodic acid, hydrofluoric acid, p-toluenesulfonic acid, methylsulfonic acid, oxalic acid, formic acid, acetic acid, hydroxyacetic acid, tartaric acid, citric acid, malic acid, malonic acid, succinic acid, glutaric acid or adipic acid.

RX(1) OF 2 A ===> B




A




● HBr

B
YIELD 91%

RX(1) RCT A 103146-25-4

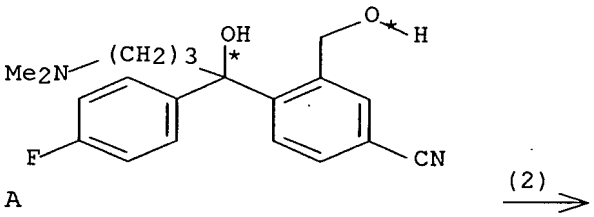
STAGE(1)
RGT C 10035-10-6 HBr
SOL 7732-18-5 Water
CON 90 deg C

STAGE(2)
SOL 141-78-6 AcOEt
CON 3 hours

STAGE(3)
SOL 7732-18-5 Water

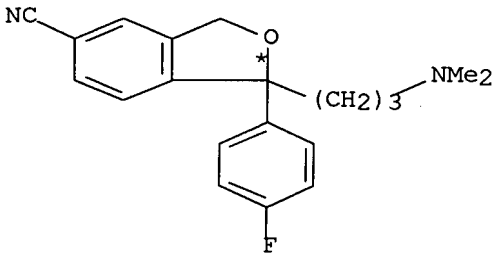
PRO B 59729-32-7
NTE second stage petroleum ether used

RX(2) OF 2 A ===> B




A

(2) →




● HBr

B
YIELD 92%

RX(2) RCT A 103146-25-4

STAGE(1)
RGT C 10035-10-6 HBr
SOL 7732-18-5 Water, 108-88-3 PhMe
CON 90 deg C

STAGE(2)
SOL 141-78-6 AcOEt
CON 3 hours

STAGE(3)
SOL 7732-18-5 Water

PRO B 59729-32-7
NTE second stage petroleum ether used

L7 ANSWER 7 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:390731 CASREACT Full-text
TITLE: Intramolecular cyclocondensation process for the preparation of citalopram and escitalopram
INVENTOR(S): Cotticelli, Giovanni; Salvetti, Raul
PATENT ASSIGNEE(S): Adorkem Technology SpA, Italy
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006037714 | A2 | 20060413 | WO 2005-EP54566 | 20050914 |
| WO 2006037714 | A3 | 20060727 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | | |
|---|---|---|---|---|
| CA 2581195 | A1 | 20060413 | CA 2005-2581195 | 20050914 |
| EP 1794140 | A2 | 20070613 | EP 2005-789627 | 20050914 |

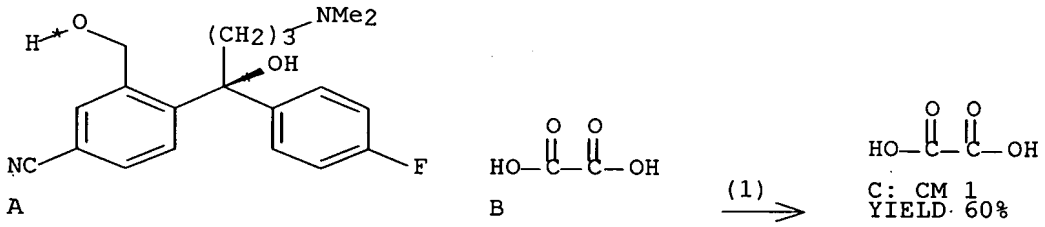
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

| | | | | |
|---|---|---|---|---|
| IN 2007DN02442 | A | 20070504 | IN 2007-DN2442 | 20070330 |
| PRIORITY APPLN. INFO.: | | | IT 2004-MI1872 | 20041001 |
| | | | WO 2005-EP54566 | 20050914 |

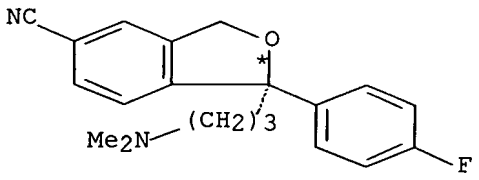
OTHER SOURCE(S): MARPAT 144:390731

AB A process is described for the preparation of citalopram and of the enantiomer escitalopram which comprises the intramol. cyclocondensation of the corresponding glycol or its chiral enantiomer using the Mitsunobu reaction with an azodicarboxylate diester, a phosphine, and a strong base.

RX(1) OF 2 A + B ===> C




A B C: CM 1
YIELD 60%



C: CM 2
YIELD 60%

RX(1) RCT A 488787-59-3

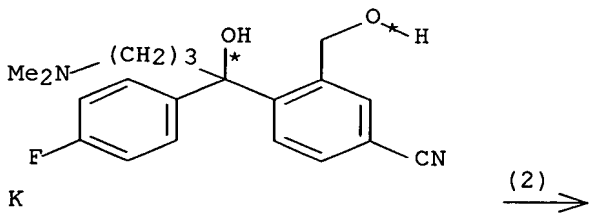
STAGE(1)
RGT D 1972-28-7 EtO2CN:NCO2Et, E 603-35-0 PPh3, F 865-48-5 NaOBu-t
SOL 109-99-9 THF
CON SUBSTAGE(2) overnight

STAGE(2)
RGT G 7647-01-0 HCl
SOL 7732-18-5 Water

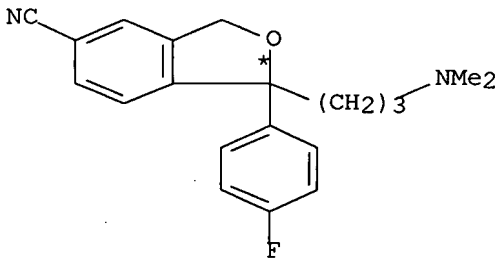
STAGE(3)
RCT B 144-62-7
SOL 67-64-1 Me2CO

PRO C 219861-08-2

RX(2) OF 2 K ===> L




K




● HBr

L
YIELD 42%

RX(2) RCT K 103146-25-4

STAGE(1)
RGT D 1972-28-7 EtO2CN:NCO2Et, E 603-35-0 PPh3, F 865-48-5 NaOBu-t
SOL 109-99-9 THF
CON SUBSTAGE(2) overnight

STAGE(2)
RGT G 7647-01-0 HCl
SOL 7732-18-5 Water

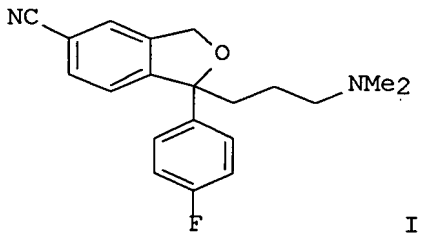
STAGE(3)
RGT M 10035-10-6 HBr
SOL 67-64-1 Me2CO
CON pH 1

PRO L 59729-32-7

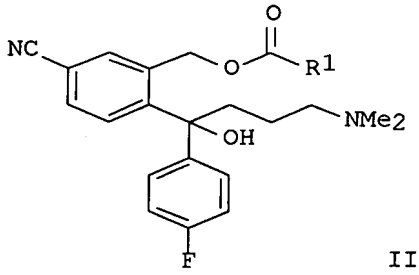
L7 ANSWER 8 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:331251 CASREACT Full-text
TITLE: Chemoenzymatic synthesis of (+)-citalopram and (-)-citalopram by kinetic resolution of diol and diol monoester intermediates using esterification or hydrolysis in the presence of Candida antarctica lipase B
INVENTOR(S): Bayod Jasanada, Miguel; Llorente Garcia, Isidro; Gotor Santamaria, Vicente; Brieva Collado, M. Rosario; Fernandez Solares, Laura; Quiros Alvarez, Margarita
PATENT ASSIGNEE(S): Astur Pharma, S.A., Spain; Universidad de Oviedo
SOURCE: Span., 14 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| ES 2228274 | A1 | 20050401 | ES 2003-2215 | 20030924 |
| ES 2228274 | B1 | 20060601 | | |

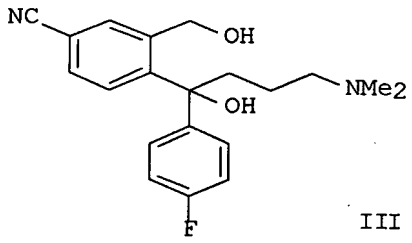
PRIORITY APPLN. INFO.: ES 2003-2215 20030924
OTHER SOURCE(S): MARPAT 144:331251
GI




I

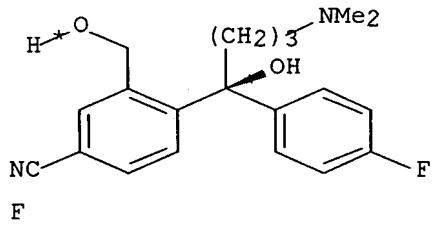



II




III

AB New processes and intermediates for the preparation of (S)-(+)- and (R)-(-)-citalopram, i.e., (+)- and (-)-I, are disclosed. The claimed intermediates include the optically enriched diol monoesters (+)- and (-)-II, as well as the diols (+)- and (-)-III [wherein: R1 = alkyl or aryl]. The claimed processes include two types of kinetic resolution: (1) enzymic acylation of racemic diol (±)-III with an acylating agent R1CO2R2 [R1 = alkyl or aryl; R2 = alkyl, alkenyl or aryl], to give (R)-(+)-II and (S)-(-)-III; and (2) enzymic hydrolysis of the racemic ester (±)-II, to give (S)-(-)-II and (R)-(+)-III. The enzyme catalyst is a hydrolase, especially a lipase, and most particularly, fraction B of the lipase of Candida antarctica (IV). Five examples are given; these cover both of the aforementioned processes, as well as hydrolysis of a monoester resolution product, and the conversion of both III enantiomers to the corresponding I enantiomers. For instance, reaction of (±)-III with vinyl acetate in MeCN in the presence of immobilized IV at 30° for 20 h gave (S)-(-)-III in 47% yield and >99% enantiomeric excess, along with some (R)-(+)-II (R1 = Me) with >90% ee. Cyclization of (S)-(-)-III by slow treatment with mesyl chloride in CH2Cl2 at 0°, followed by stirring for 1 h at 15°, gave (S)-(+)-I in 90% yield and >99% ee.



F

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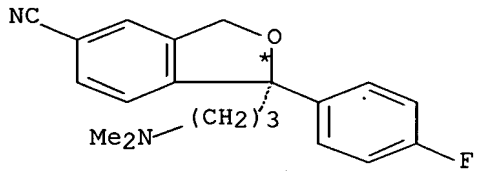
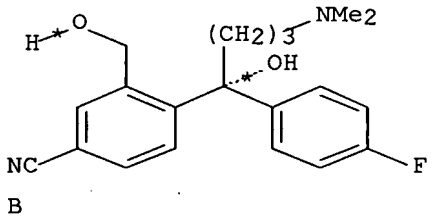


G
YIELD 90%

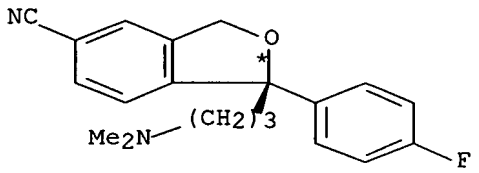
RX(2)
RCT F 488787-59-3
RGT H 124-63-0 MeSO2Cl
PRO G 128196-01-0
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> 15 deg C
SUBSTAGE(3) 1 hour, 15 deg C
NTE product ee >99%

RX(3) OF 10 ...B ===> J



B

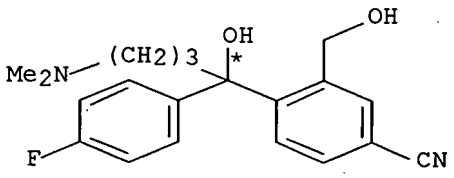
(3) →



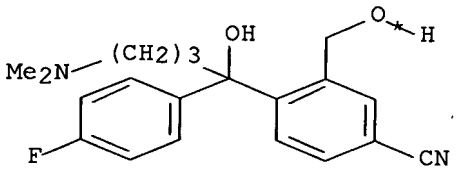
J
YIELD 90%

RX(3)  RCT  B 481047-48-7
       RGT  H 124-63-0 MeSO2Cl
       PRO  J 128196-02-1
       SOL  75-09-2 CH2Cl2
       CON  SUBSTAGE(1) 0 deg C
            SUBSTAGE(2) 0 deg C -> 15 deg C
            SUBSTAGE(3) 1 hour, 15 deg C
       NTE  product ee >99%

RX(9) OF 10 COMPOSED OF RX(4), RX(2)
RX(9)  2 K + L ===> G




K

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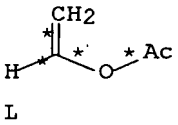
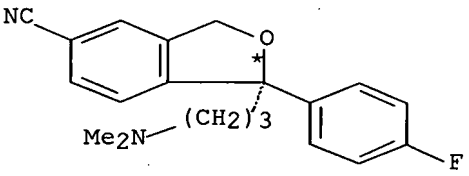



L

2
STEPS



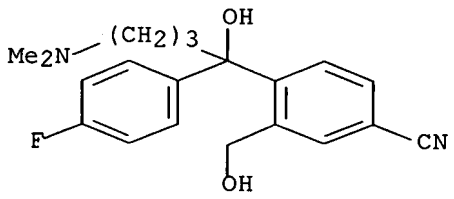

G
YIELD 90%

RX(4)  RCT  K 103146-25-4, L 108-05-4
       PRO  A 674806-13-4, F 488787-59-3
       CAT  9001-62-1 Lipase
       SOL  75-05-8 MeCN
       CON  20 hours, 30 deg C
       NTE  enzymic, solid-supported catalyst, ee of diol >99%, ee of monoester >90%

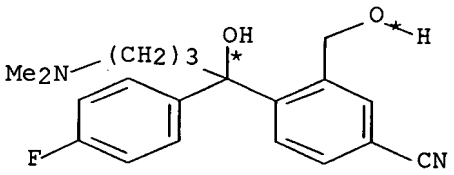
RX(2)  RCT  F 488787-59-3
       RGT  H 124-63-0 MeSO2Cl
       PRO  G 128196-01-0
       SOL  75-09-2 CH2Cl2
       CON  SUBSTAGE(1) 0 deg C

SUBSTAGE(2) 0 deg C -> 15 deg C
SUBSTAGE(3) 1 hour, 15 deg C
NTE product ee >99%

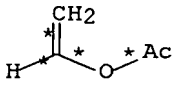
RX(10) OF 10 COMPOSED OF RX(4), RX(1), RX(3)
RX(10) 2 K + L ===> J




K

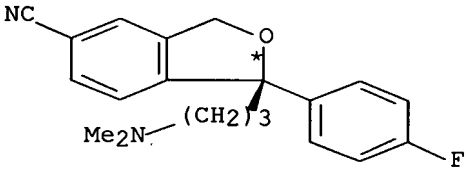



K




L

3
STEPS




J
YIELD 90%

RX(4) RCT K 103146-25-4, L 108-05-4
PRO A 674806-13-4, F 488787-59-3
CAT 9001-62-1 Lipase
SOL 75-05-8 MeCN
CON 20 hours, 30 deg C
NTE enzymic, solid-supported catalyst, ee of diol >99%, ee of monoester >90%

RX(1) RCT A 674806-13-4
RGT C 7732-18-5 Water, D 1310-73-2 NaOH
PRO B 481047-48-7
SOL 67-56-1 MeOH
CON 12 hours, room temperature
NTE ee of product >99%

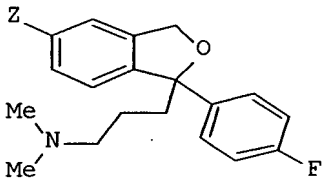
RX(3) RCT B 481047-48-7
RGT H 124-63-0 MeSO2Cl
PRO J 128196-02-1
SOL 75-09-2 CH2Cl2

CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> 15 deg C
SUBSTAGE(3) 1 hour, 15 deg C
NTE product ee >99%

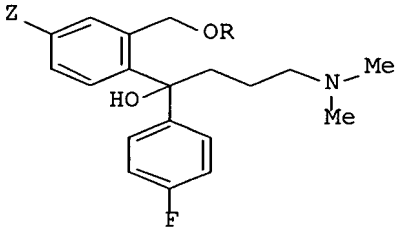
L7 ANSWER 9 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:274127 CASREACT Full-text
TITLE: Process for preparation of citalopram and its enantiomers via acid or base cyclization of the diol
INVENTOR(S): Periyandi, Nagarajan; Kilaru, Srinivasu; Thennati, Rajamannar
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006021971 | A2 | 20060302 | WO 2005-IN276 | 20050812 |
| WO 2006021971 | A3 | 20060713 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| IN 2004MU00912 | A | 20070420 | IN 2004-MU912 | 20040823 |
| EP 1797060 | A2 | 20070620 | EP 2005-815687 | 20050812 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |

PRIORITY APPLN. INFO.: IN 2004-MU912 20040823
WO 2005-IN276 20050812
OTHER SOURCE(S): MARPAT 144:274127
GI



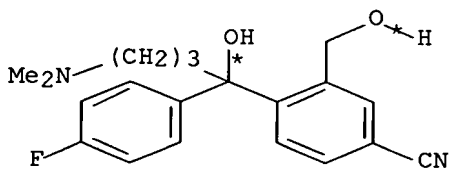
I



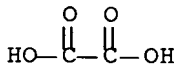
II

AB The invention provides a process for preparation of 1-[3-(dimethylamino)propyl]- 1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile I (Z = CN; citalopram) and its enantiomers. The process for preparation of compound I comprising reacting a compound of formula II (R = H), in the presence of a base, with a compound of formula RX, wherein R is (un)substituted alkyl, (un)substituted alkenyl, and (un)substituted (hetero)aryl; X is from F, Cl, Br, I, CN, OTf and OR1; R1 is (un)substituted alkyl; Z is CN or a group that may be converted to a cyano group; so that an intermediate ether derivative, where R is as defined above, is formed from said reaction, which ether cyclizes to give a compound of formula I, where Z is not a cyano group, and conversion of the group Z in the compound of formula I to a cyano group to form racemic I (Z = CN), is claimed in this invention. The invention also provides ether compds., compds. of formula II and a process for preparation thereof. (S)-(+)-Citropram, i.e., (S)-(+)-I (Z = CN) was prepared by nucleophilic aromatic substitution of 2,5-dichloronitrobenzene with (S)-(-)-II (Z = CN; R = H) to give the corresponding benzylic Ph ether, that was converted to its HCl salt, and cyclized in the presence of potassium carbonate to give (S)-(+)-I.

RX(1) OF 9 A + B ===> C

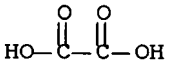



A

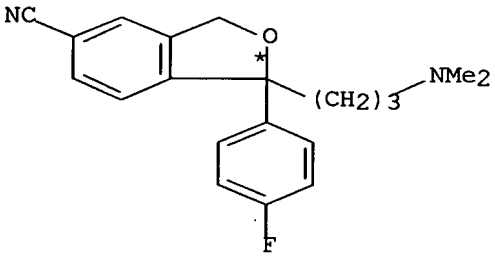



B

(1) ⟶




C: CM 1




C: CM 2

RX(1) RCT A 103146-25-4

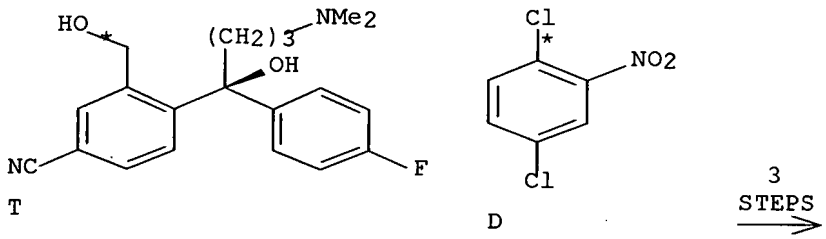
STAGE(1)
RGT D 89-61-2 Benzene, 1,4-dichloro-2-nitro-, E 584-08-7 K2CO3
SOL 67-68-5 DMSO
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 15 hours, 100 deg C

STAGE(2)
RGT F 1310-73-2 NaOH, G 12408-02-5 H+
SOL 7732-18-5 Water

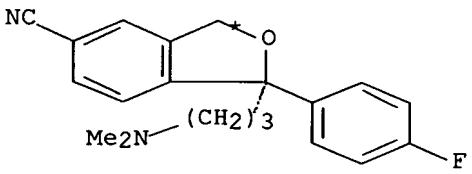
STAGE(3)
RCT B 144-62-7
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 30 deg C
SUBSTAGE(2) cooled

PRO C 207559-01-1

RX(9) OF 9 COMPOSED OF RX(6), RX(4), RX(5)
RX(9) T + D ===> S




T D




S

RX(6) RCT T 488787-59-3

STAGE(1)
RGT M 865-47-4 t-BuOK
SOL 109-99-9 THF
CON 10 minutes, 0 - 10 deg C

STAGE(2)
RCT D 89-61-2
CON SUBSTAGE(1) 0 - 10 deg C
SUBSTAGE(2) 10 - 15 hours, 30 - 35 deg C

STAGE(3)
RGT F 1310-73-2 NaOH
SOL 7732-18-5 Water

PRO O 878042-63-8

RX(4) RCT O 878042-63-8
RGT Q 7647-01-0 HCl
PRO P 878007-22-8
SOL 67-63-0 Me2CHOH
CON 30 deg C

RX(5) RCT P 878007-22-8
RGT E 584-08-7 K2CO3
PRO S 128196-01-0
SOL 67-68-5 DMSO
CON SUBSTAGE(1) 30 - 35 deg C
SUBSTAGE(2) 30 minutes, 95 - 100 deg C

L7 ANSWER 10 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:248161 CASREACT Full-text
TITLE: Method for the separation of intermediates which may be used for the preparation of escitalopram
INVENTOR(S): Lyngso, Lars Ole
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005077891 | A1 | 20050825 | WO 2005-DK75 | 20050202 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2005212455 | A1 | 20050825 | AU 2005-212455 | 20050202 |
| CA 2555980 | A1 | 20050825 | CA 2005-2555980 | 20050202 |
| EP 1716108 | A1 | 20061102 | EP 2005-700625 | 20050202 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU | | | | |
| CN 1918112 | A | 20070221 | CN 2005-80004594 | 20050202 |
| BR 2005007580 | A | 20070731 | BR 2005-7580 | 20050202 |
| JP 2007524678 | T | 20070830 | JP 2006-552461 | 20050202 |
| MX 2006PA08977 | A | 20061020 | MX 2006-PA8977 | 20060808 |
| IN 2006CN02945 | A | 20070608 | IN 2006-CN2945 | 20060810 |
| NO 2006004086 | A | 20060912 | NO 2006-4086 | 20060912 |

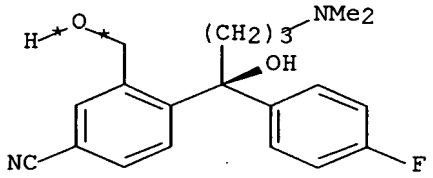
US 2007190624 A1 20070816 US 2006-597836 20061108
PRIORITY APPLN. INFO.: DK 2004-217 20040212
US 2004-544970P 20040212
WO 2005-DK75 20050202
OTHER SOURCE(S): MARPAT 143:248161
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

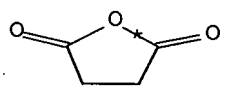
AB Compds. I [R1 = H, or group II; R2 = CN, or a group which may be converted to CN; R3 = halo; X = double or single bond; Y = bond, O, S, or NH; W = O, or S; R4 = alkyl, alkenyl, alkynyl, aryl, hetroaryl, all of which may be optionally substituted with alkoxy, alkythio, halo, OH, NH, NO2, CN, alkylamino, aryl, aryloxy, arylthio, and heteroaryl], or a salt from a mixture of I [R1 = group II] and I [R1 = H], which was reacting with cyclic anhydride or imide to form a mixture of I [R1 = group II] and an esters III (R5 = substituted heteroaryl carboxylic acid), were prepared by enzymic acylation or deacylation, separated, isolated and purified and used for manufacturing of escitalopram and derivs. Compds. I [R1 = group II] were separated from esters III by precipitation of III from the mixture, or by partitioning between an organic solvent and aqueous solvent, by adsorbing I [R1 = group II] on a basic resin. Thus, addition of succinic anhydride to a mixture of butyric acid 5-cyano-2-[4-dimethylamino-1-(4-fluorophenyl)-1-hydroxybutyl]-benzyl ester and prepared by enzymic resolution 4-[(S)-4-dimethylamino-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile, gave after precipitation and washing 2,02 g of escitalopram [(S)-1-(3-dimethylamino-propyl)-1-(4-fluoro-phenyl)- 1,3-dihydro-isobenzofuran-5-carbonitrile] hydrogen oxalate (ee = 95%).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

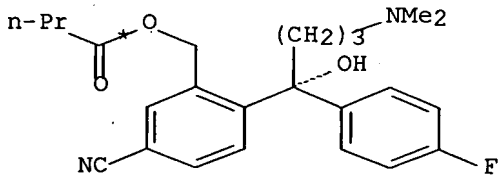
RX(4) OF 6 COMPOSED OF RX(1), RX(2)
RX(4) A + 2 B + C + F ===> G



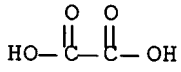

A




2 B

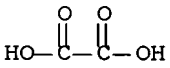



C

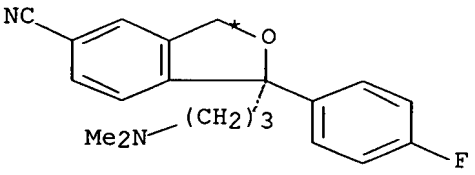



F

2 STEPS →



G: CM 1



G: CM 2

RX(1) RCT A 488787-59-3, B 108-30-5, C 658080-70-7
PRO D 863116-45-4
SOL 109-99-9 THF
CON overnight, room temperature

RX(2) RCT D 863116-45-4

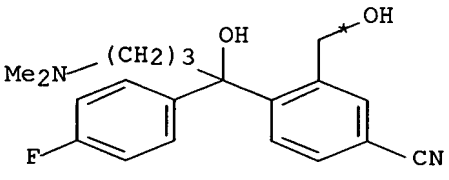
STAGE(1)
RGT H 7646-69-7 NaH
SOL 68-12-2 DMF
CON overnight, room temperature

STAGE(2)
RGT I 7732-18-5 Water
CON room temperature

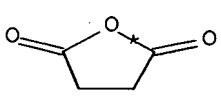
STAGE(3)
RCT F 144-62-7
SOL 67-64-1 Me2CO
CON 1 hour, room temperature

PRO G 219861-08-2

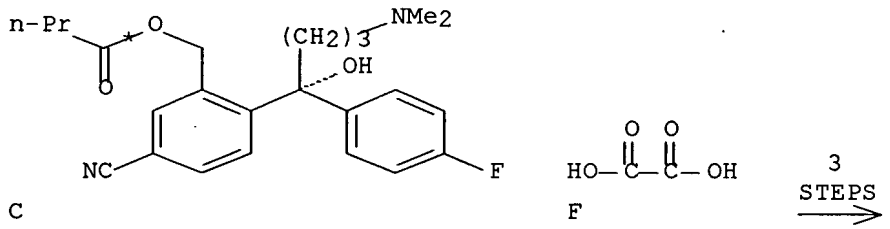
RX(6) OF 6 COMPOSED OF RX(3), RX(1), RX(2)
RX(6) L + 2 B + C + F ===> G



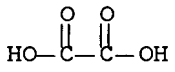
L



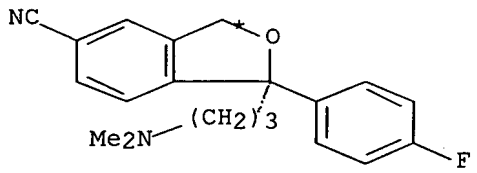
2 B




C F




G: CM 1




G: CM 2

RX(3) RCT L 103146-25-4
RGT M 123-20-6 Butanoic acid, ethenyl ester
PRO A 488787-59-3
CAT 9004-02-8 Lipase, lipoprotein
SOL 123-91-1 Dioxane
CON SUBSTAGE(1) room temperature -> 50 deg C
SUBSTAGE(2) 192 hours, 50 deg C
SUBSTAGE(3) 504 hours, 50 deg C
NTE biotransformation, enzymic, stereoselective, lipoptrotein lipase from Pseudomonas sp. used

RX(1) RCT A 488787-59-3, B 108-30-5, C 658080-70-7
PRO D 863116-45-4
SOL 109-99-9 THF
CON overnight, room temperature

RX(2) RCT D 863116-45-4

STAGE(1)
RGT H 7646-69-7 NaH
SOL 68-12-2 DMF
CON overnight, room temperature

STAGE(2)
RGT I 7732-18-5 Water
CON room temperature

STAGE(3)

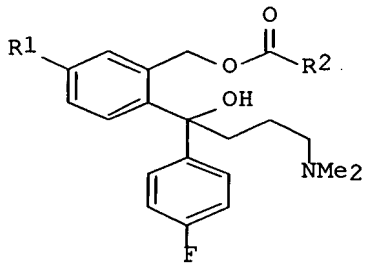
RCT F 144-62-7
SOL 67-64-1 Me2CO
CON 1 hour, room temperature

PRO G 219861-08-2

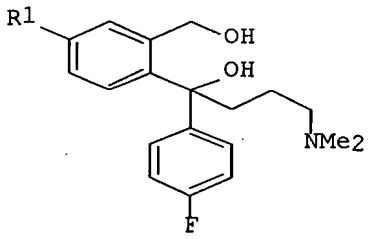
L7 ANSWER 11 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:59681 CASREACT Full-text
TITLE: Process for the preparation of citalopram enantiomer
INVENTOR(S): Li, Lan; Li, Qian
PATENT ASSIGNEE(S): Dezhong Wanquan Pharmaceutical Technology Developing Co., Ltd., Beijing, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| CN 1510024 | A | 20040707 | CN 2002-158181 | 20021224 |
| PRIORITY APPLN. INFO.: | | | CN 2002-158181 | 20021224 |

OTHER SOURCE(S): MARPAT 143:59681
GI



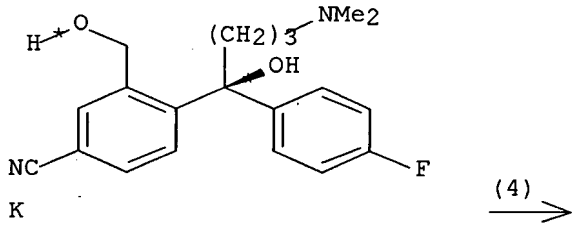

I




II

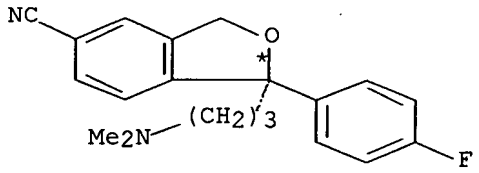
AB A process for the preparation of title compound, a drug as antidepressant, and the preparation of its intermediate I [R1 = CN, halo, alkoxy, alkylaminocarbonyl; R2 = amino containing group, amino containing aryl or cyclic ring] comprising reacting a compound of formula II with a compound of formula XCOR2 (R1, R2 are defined as above) is disclosed. For example, reaction of II (R1 = CN) with 2-chloronicotinic acid gave I (R1 = CN, R2 = 2-chloropyridin-3-yl) in 80% yield. Optical resolution of I by salification of I with di-p-toluoyl-L-tartaric acid , followed by recrystn. and hydrolysis, provided (S)-II. Cyclization of (S)-II gave optical active (S)-citalopram.

RX(4) OF 10 ...K ===> P




K

(4) →




P

RX(4) RCT K 488787-59-3

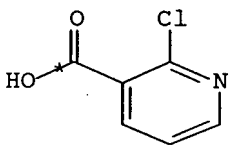
STAGE(1)
RGT D 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT Q 98-59-9 TsCl
SOL 75-09-2 CH2Cl2
CON 3 hours, 0 deg C

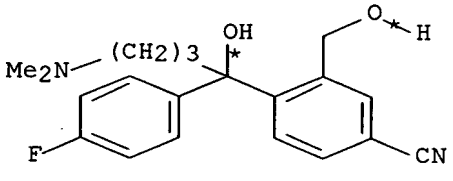
STAGE(3)
RGT R 144-62-7 (CO2H)2
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 1 hour, reflux
SUBSTAGE(2) overnight, reflux -> room temperature

PRO P 128196-01-0

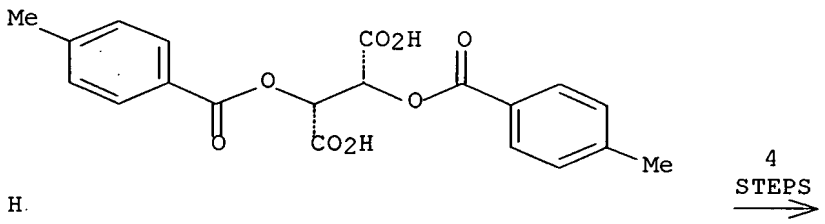
RX(10) OF 10 COMPOSED OF RX(1), RX(2), RX(3), RX(4)
RX(10) A + B + H ===> P




A

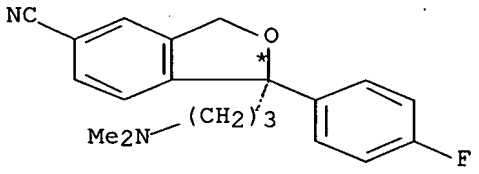



B




H

4
STEPS




P

RX(1) RCT A 2942-59-8

STAGE(1)
SOL 7719-09-7 SOCl2
CON 2 hours, reflux

STAGE(2)
RCT B 103146-25-4
SOL 75-09-2 CH2Cl2

STAGE(3)
RGT D 121-44-8 Et3N
CON 16 hours, room temperature

STAGE(4)
SOL 108-20-3 Isopropyl ether
CON 2 hours, room temperature

PRO C 853904-55-9

RX(2) RCT C 853904-55-9, H 32634-66-5
PRO I 853904-57-1
SOL 67-63-0 Me2CHOH
CON SUBSTAGE(1) 0.5 hours, reflux
SUBSTAGE(2) overnight, reflux -> room temperature
NTE stereoselective

RX(3) RCT I 853904-57-1

STAGE(1)
RGT L 497-19-8 Na2CO3
SOL 7732-18-5 Water
CON room temperature, pH 8 - 9

STAGE(2)

SOL 108-20-3 Isopropyl ether
CON 2 hours, room temperature

STAGE(3)
RGT M 1310-73-2 NaOH
SOL 7732-18-5 Water, 64-17-5 EtOH
CON 8 hours, room temperature

PRO K 488787-59-3

RX(4) RCT K 488787-59-3

STAGE(1)
RGT D 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT Q 98-59-9 TsCl
SOL 75-09-2 CH2Cl2
CON 3 hours, 0 deg C

STAGE(3)
RGT R 144-62-7 (CO2H)2
SOL 67-64-1 Me2CO
CON SUBSTAGE(1) 1 hour, reflux
SUBSTAGE(2) overnight, reflux -> room temperature

PRO P 128196-01-0

L7 ANSWER 12 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:197860 CASREACT Full-text
TITLE: Process for purification of citalopram via washing with polybasic acid solutions
INVENTOR(S): Uttarwar, Sunil Govindrao; Gawli, Bhagwan Narayan
PATENT ASSIGNEE(S): Meditab Specialities Pvt. Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

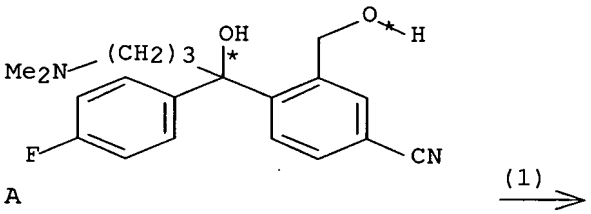
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005012278 | A2 | 20050210 | WO 2004-GB3209 | 20040723 |
| WO 2005012278 | A3 | 20050616 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

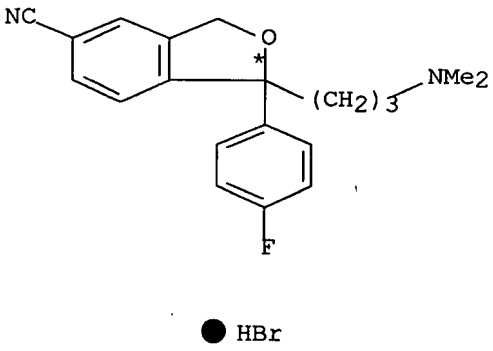
| | | | | |
|---|---|---|---|---|
| GB 2418916 | A | 20060412 | GB 2006-1023 | 20040723 |
| DE 112004001368 | T5 | 20060629 | DE 2004-112004001368 | 20040723 |
| IN 2006MN00092 | A | 20061006 | IN 2006-MN92 | 20060124 |
| US 2006189816 | A1 | 20060824 | US 2006-565736 | 20060419 |
| PRIORITY APPLN. INFO.: | | | GB 2003-17475 | 20030725 |
| | | | WO 2004-GB3209 | 20040723 |

AB A process for purification of racemic or optically active citalopram (I) comprises (i) providing crude I containing ≥1 I derivs. dissolved in a H2O-immiscible organic solvent, (ii) washing the crude mixture with ≥1 dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to sep. I from impurities present in the crude mixture; and (iii) where required converting purified I free base to a pharmaceutically acceptable salt. Thus, 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile was heated at 105° in aqueous H3PO4 followed by cooling, dilution with H2O, pH adjustment to 8-10 with aqueous NH3, and extraction with EtOAc. The EtOAc layer was washed with aqueous disodium edetate followed by drying over Na2SO4, treatment with decolorizing C, and filtration to give >99.85% pure citalopram hydrobromide.

RX(1) OF 3 A ===> B




A




B

RX(1) RCT A 103146-25-4

STAGE(1)
RGT C 7664-38-2 H3PO4
SOL 7732-18-5 Water

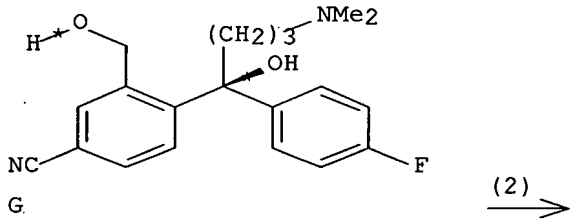
CON 14 hours, 105 deg C

STAGE(2)
RGT D 7664-41-7 NH3
SOL 7732-18-5 Water
CON 40 deg C, pH 8 - 10

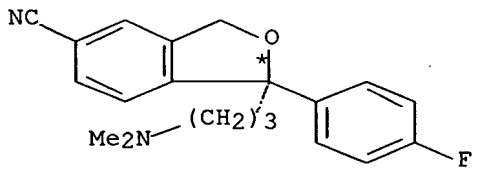
STAGE(3)
RGT E 10035-10-6 HBr
SOL 7732-18-5 Water
CON room temperature, pH 3 - 3.5

PRO B 59729-32-7

RX(2) OF 3 G ===> H




G




H

RX(2) RCT G 488787-59-3

STAGE(1)
SOL 75-09-2 CH2Cl2
CON room temperature -> 0 deg C

STAGE(2)
RGT I 124-63-0 MeSO2Cl, J 121-44-8 Et3N
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 2 hours, 5 deg C

STAGE(3)
RGT K 144-62-7 (CO2H)2
SOL 67-64-1 Me2CO
CON 1 hour, 10 deg C

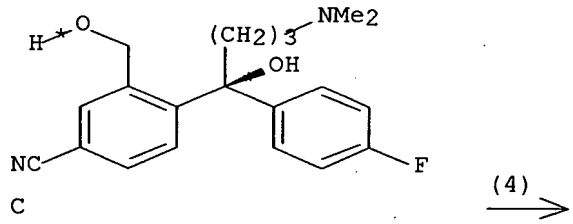
PRO H 128196-01-0

L7 ANSWER 13 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:287145 CASREACT Full-text
TITLE: Enzymatic resolution of a quaternary stereogenic center as the key step in the synthesis of (S)-(+)-citalopram
AUTHOR(S): Solares, Laura F.; Brieva, Rosario; Quiros, Margarita; Llorente, Isidro; Bayod, Miguel; Gotor, Vicente
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Facultad de Quimica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Tetrahedron: Asymmetry (2004), 15(2), 341-345
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

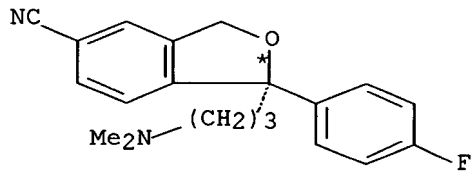
AB The enzymic resolution of 4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile, a useful intermediate in the synthesis of enantiomerically pure citalopram, has been studied. Candida antarctica lipase B (CAL-B) catalyzes the enzymic acetylation of the primary benzylic alc. with high enantioselectivity at the quaternary stereogenic center. This enzymic acetylation yielded the acetylated (+)-3-[(acetyloxy)methyl]-4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]benzonitrile and the desired (-)-4-[(1S)-4-(dimethylamino)-1- (4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile. The enzymic enantioselective hydrolysis of the 3-acetyloxymethyl derivative catalyzed by CAL-B is also possible.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(4) OF 6 ...C ===> N




C

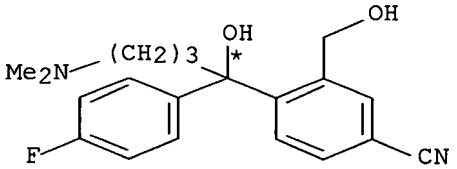



N
YIELD 90%

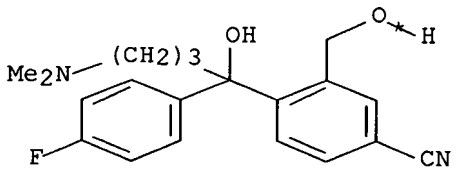
RX(4) RCT C 488787-59-3
RGT O 124-63-0 MeSO2Cl
PRO N 128196-01-0

SOL 75-09-2 CH2Cl2
CON 1 hour, 0 deg C -> 15 deg C

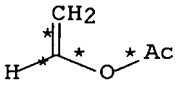
RX(6) OF 6 COMPOSED OF RX(1), RX(4)
RX(6) 2 A + B ===> N



A

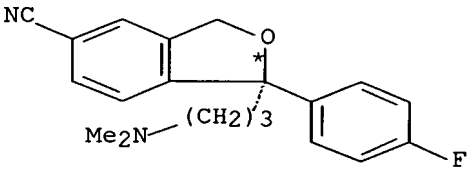


A



B

2
STEPS



N
YIELD 90%

RX(1) RCT A 103146-25-4, B 108-05-4
PRO C 488787-59-3, D 674806-13-4
CAT 9001-62-1 Lipase
SOL 75-05-8 MeCN
CON 21 hours, 30 deg C
NTE biotransformation, enzymic, stereoselective, lipase B from Candida antarctica, optimization study, optimized on concentration,solvent

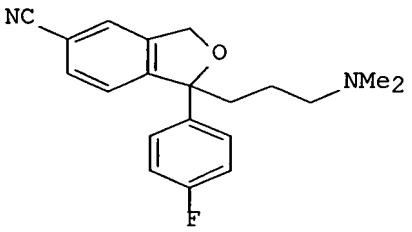
RX(4) RCT C 488787-59-3
RGT O 124-63-0 MeSO2Cl
PRO N 128196-01-0
SOL 75-09-2 CH2Cl2
CON 1 hour, 0 deg C -> 15 deg C

L7 ANSWER 14 OF 14 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:73169 CASREACT Full-text
TITLE: Preparation of racemic citalopram and/or S- or R-citalopram by separation of a mixture of R- and S-citalopram

INVENTOR(S): Humble, Rikke Eva; Christensen, Troels Volsgaard; Rock, Michael Harold; Nielsen, Ole; Petersen, Hans; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003000672 | A1 | 20030103 | WO 2002-DK426 | 20020625 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EG 22991 | A | 20031231 | EG 2002-725 | 20020624 |
| CA 2450890 | A1 | 20030103 | CA 2002-2450890 | 20020625 |
| AU 2002344948 | A1 | 20030108 | AU 2002-344948 | 20020625 |
| AU 2002344948 | B2 | 20070816 | | |
| EP 1412341 | A1 | 20040428 | EP 2002-742848 | 20020625 |
| EP 1412341 | B1 | 20041208 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2002010574 | A | 20040803 | BR 2002-10574 | 20020625 |
| CN 1520405 | A | 20040811 | CN 2002-812668 | 20020625 |
| HU 200400293 | A2 | 20040928 | HU 2004-293 | 20020625 |
| HU 200400293 | A3 | 20070529 | | |
| JP 2004536093 | T | 20041202 | JP 2003-507077 | 20020625 |
| AT 284395 | T | 20041215 | AT 2002-742848 | 20020625 |
| PT 1412341 | T | 20050429 | PT 2002-742848 | 20020625 |
| ES 2233834 | T3 | 20050616 | ES 2002-2742848 | 20020625 |
| TW 236473 | B | 20050721 | TW 2002-91113845 | 20020625 |
| NZ 530104 | A | 20060831 | NZ 2002-530104 | 20020625 |
| ZA 2003009633 | A | 20041213 | ZA 2003-9633 | 20031211 |
| MX 2003PA11770 | A | 20040402 | MX 2003-PA11770 | 20031217 |
| BG 108532 | A | 20050430 | BG 2004-108532 | 20040114 |
| IN 2004CN00142 | A | 20051209 | IN 2004-CN142 | 20040123 |
| US 2004259940 | A1 | 20041223 | US 2004-482000 | 20040209 |
| US 7112686 | B2 | 20060926 | | |
| PRIORITY APPLN. INFO.: | | | DK 2001-991 | 20010625 |
| | | | WO 2002-DK426 | 20020625 |

GI

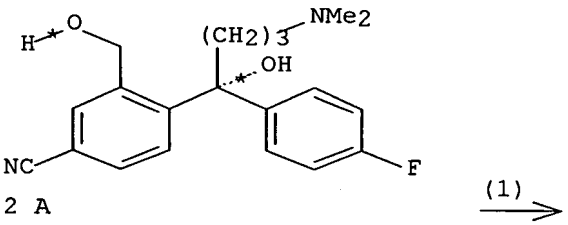


I

AB Citalopram (I), free base or an acid addition salt thereof, and/or R- or S-citalopram as the free base or an acid addition salt thereof, were prepared by separation of a mixture of R- and S-citalopram with more than 50% of one of the enantiomers into a fraction consisting of racemic citalopram and/or a fraction of S-citalopram or R-citalopram. The mixture of R- and S-citalopram was generally prepared by acid- or base-catalyzed ring closure of R- or S-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile. Racemic citalopram and S-citalopram are well-known antidepressants (no data).

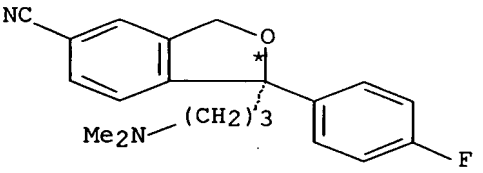
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 2 A ===> B + C

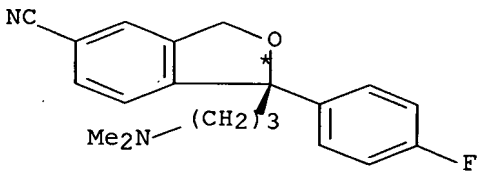


2 A

(1)



B
YIELD 99%(73)



C
YIELD 99%(27)

RX(1) RCT A 481047-48-7
RGT D 7664-93-9 H2SO4
PRO B 128196-01-0, C 128196-02-1
SOL 7732-18-5 Water, 75-05-8 MeCN
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 3 hours, 78 - 85 deg C
NTE optimization study

```
=> save l7 temp cott10577869/a
ANSWER SET L7 HAS BEEN SAVED AS 'COTT10577869/A'

=> logoff h
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   227.42     229.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -10.22     -10.22

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 18:54:24 ON 28 SEP 2007
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# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 2744 | citalopram | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:52 |
| L2 | 34 | L1 and (methane adj sulfonyl) | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 18:06 |
| L6 | 494 | citalopram and cyclization | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 19:04 |
| L7 | 239 | diol and (methane$2sulfonyl$2chloride) | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:55 |
| L8 | 495 | l6 andl7 | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:55 |
| L9 | 0 | l6 and l7 | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:57 |
| L10 | 219 | "4136193" | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:57 |
| L11 | 0 | "4136193.pn." | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:57 |
| L12 | 4 | "4136193".pn. | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:57 |

# EAST Search History

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|---|---|---|---|---|---|---|
| L13 | 2 | "4,650,884".pn. | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 18:19 |
| L14 | 2 | "4943590".pn. | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 18:19 |
| L15 | 97 | l6 and triphenylphosphine | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 19:05 |
| S1 | 94 | 5-cyanophthalide | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:52 |
| S2 | 66074 | phosphine | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:51 |
| S3 | 99 | S1 andl2 | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:52 |
| S4 | 2722 | citalopram | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/28 17:54 |
| S5 | 103 | S3 andl4 | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:53 |
| S6 | 82 | S3 and S4 | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:54 |
| S7 | 51 | cotticelli | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:54 |

# EAST Search History

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|---|---|---|---|---|---|---|
| S8 | 9 | S6 and S7 | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:57 |
| S9 | 41 | 5-carboxyphthalide | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:57 |
| S10 | 20 | S9 and S1 | US-PGPUB; USPAT; FPRS; EPO; JPO; DERWENT | OR | ON | 2007/09/12 19:57 |